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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/757,555	01/09/2001	Levon Michael Khachigian	273402002020	9700

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EXAMINER	
EPPS, JANET L	

ART UNIT	PAPER NUMBER
1635	15

DATE MAILED: 01/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/757,555	KHACHIGIAN, LEVON MICHAEL	
	Examiner	Art Unit	
	Janet L Epps-Ford, Ph.D.	1635	

-- Th MAILING DATE of this communication app ars on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 4-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/142,779* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Drawings

2. Applicants have not responded to the request for corrected drawings as set forth in the prior Office Action mailed 4-23-02 which stated that "[I]n order to avoid abandonment, the drawing informalities noted in the PTO-948 attached to Paper No. 4, mailed on 7-31-01, must now be corrected." Correction can only be effected in the manner set forth in the above noted paper.

Response to Amendment

3. The Declaration filed under 37 CFR 1.132 filed 10-23-02 is insufficient to overcome the rejection of claims 1-2 based upon 35 USC 102(b) and the rejection of claims 1-3 under 35 USC 103(a) as obvious over Mendelsohn et al. as set forth in the last Office action because the facts presented are not germane to the rejection at issue. See MPEP § 716, and the reasons set forth below.

Claim Rejections - 35 USC § 102

4. Claims 1-2 remain rejected and claims 4-9 are rejected under 35 USC 102(b) as being anticipated by Hu et al. for the reasons of record set forth in the Official Action mailed 4-23-02.

Applicant's arguments filed 10-23-02 have been fully considered but they are not persuasive. Applicants traverse the instant rejection based upon the evidence provided in the Declaration of Dr. Khachigian. According to Applicants the Declaration of Khachigian consistently teaches that the claims are directed to a method of screening for compounds, which

can inhibit proliferation of vascular, and neoplasia cells, wherein the compounds are selected by their ability to inhibit Egr-1. However, contrary to Applicant's assertions, the instant claims read on a method of screening for compounds that inhibit proliferation of cells selected from the group consisting of vascular cells and neoplasia cells, the method comprising determining the ability of a putative compound to inhibit induction of Egr-1, decrease expression of Egr-1 or decrease the nuclear accumulation or activity of the Egr-1 gene product wherein the method is performed *in vitro*, and further wherein the vascular cells are selected from the group consisting of smooth muscle cells and endothelial cells. The recitation of the phrase "method of screening for compounds that inhibit proliferation of cells," in the preamble of claim 1, merely represents the intended use of the claimed method. The method steps of Applicant's recited method clearly are anticipated by the teachings of Hu et al.

Applicants have not provided any evidence that would suggest that Hu et al. does not teach a method for screening the ability of a putative compound to inhibit the induction of Egr-1. Although, applicants may argue that the compounds of Hu et al. do not inhibit or regulate Egr-1 expression, the teachings of Hu et al. clearly disclose a screen for determining the ability of a putative compound to inhibit Egr-1 expression. Despite what the specification as filed teaches, the claims clearly recite a method for screening compounds, comprising the testing of putative compounds, which indicates that it is not required that the proposed test compound (i.e. putative compound) actually functions as an inhibitor, the purpose of the screen is to identify inhibitors, not to start with an inhibitor and then to screen for its ability to inhibit, such a screen would be redundant.

Additionally, Hu et al. teach that ANP and endothelin normally functions to control Tis-8 expression in cultured glia cells, however, because the glioma cells are cancerous, the normal regulation of egr-1 is somehow disrupted as in Wilm's tumors. Furthermore, Hu et al. states that additional studies are needed to understand the mechanism of the loss of Tis-8 regulation by ANP and ET in glioma cells (page 1826, paraphrasing paragraph 5). Hu et al. clearly discloses a method for screening the ability of ANP and ET to regulate Tis-8 or (EGR-1) in glioma cells.

Claim Rejections - 35 USC § 103

5. Claims 1-2 remain rejected and claims 4-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mendelsohn et al. for the reasons of record set forth in the Official action mailed 4-23-02.

Applicant's arguments filed 10-23-02 have been fully considered but they are not persuasive. Applicants traverse the instant rejection over Mendelsohn et al. on the grounds that the disclosure of this reference teaches "away from screening for agents that inhibit 'estrogen responsive genes in vascular cells.'" First it is noted that the instant claims do not specifically recite a method for "screening for agents that inhibit 'estrogen responsive genes in vascular cells.'" The recitation of the phrase "method of screening for compounds that inhibit proliferation of cells," in the preamble of claim 1, merely represents the intended use of the claimed method.

Mendelsohn et al. clearly provides screening methods that can be used to identify vasoprotective agents, wherein preferred vasoprotective agents are identified by their ability to influence the expression of an estrogen responsive gene. In one specific embodiment Mendelson et al. teaches that a vasoprotective agent can be identified by assaying its ability to inhibit or

decrease the expression of egr-1, indicated by egr-1 (-/-) (see col. 11, line 54). Mendelsohnn et al. does not explicitly describe a method of screening for compounds that inhibit proliferation of cells selected from vascular smooth muscle cells or endothelial cells, wherein the method specifically comprises determining the ability of a putative compound to inhibit induction of egr-1. However, Mendelsohnn et al. clearly teach that "any gene which is responsive to an estrogen receptor can serve as the basis for a reporter construct (col. 11, lines 22-23)," wherein said reporter constructs are "used to indirectly monitor the effect of an agent on the proliferation and/or activation of vascular cells and to monitor the effect of an agent on the expression of an estrogen responsive gene (col. 11, lines 12-15)." Mendelsohnn et al. goes on to describe vascular genes of interest to be used in said reporter constructs, wherein the list of vascular genes comprises the "egr-1" gene (col. 11, lines 29). Additionally, Mendelsohnn et al. specifically teaches that the expected effect of the potential vasoproctective agent on the expression of egr-1 is a decrease (-/-) in expression of egr-1 in both vascular smooth muscle cells and vascular endothelial cells (col. 11, lines 46-54).

The Declaration of Dr. Kachigian merely argues that "no molecular or cellular biological rationale is provided in the document as to why the expression of Egr-1 should be increased or decreased by the preferred agent, beyond a mere responsiveness to estrogen." The arguments of Dr. Kachigian provides no evidence or rationale to obviate the clear teachings of Mendelsohn et al. which clearly provides a method for identifying agents comprising screening the ability of a putative agent to decrease expression of egr-1 in vascular endothelial and vascular smooth muscle cells (col. 11, lines 46-54).

Conclusion

6. THIS **ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps-Ford, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Friday 9:00AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE
December 31, 2002

SEAN McGARRY
PRIMARY EXAMINER